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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,225	10/31/2003	Dan-Hui Dorothy Yang	10021166-1	1504

7590 03/13/2006

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EXAMINER	
HAQ, SHAFIQUL	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,225	YANG ET AL.	
	Examiner	Art Unit	
	Shafiqul Haq	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/26/05 has been entered.
2. Claims 1-20 are pending and under active prosecution.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1, 7-12, and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butler et al (US 6,589,726 B1) in view of Lefkowitz et al (US 6,258,454 B1).

Butler et al reference teaches a solid support array with hydrophilic sites that are spatially segregated by hydrophobic sites (i.e. intervening areas), wherein the hydrophilic sites contain free amino, hydroxyl, carboxyl, thiol and amido groups (i.e.

surface modification) that can support non-covalent attachment to biological entities including molecule (i.e. probe not forming a covalent bond and non-covalently attached to the substrate), and wherein solutions of reactants are added to hydrophilic sites using the drop-on-demand method that is analogous to the inkjet printing technology (i.e. depositing solutions onto discrete sites), wherein the support can comprise a library of molecules (i.e. providing at least two solutions, each solution comprising a probe; probe that is different from at least one other probe in another solution), and wherein the reactions on the support can be protein-protein interactions (i.e. protein array wherein probe is a protein). See column 6, lines 11-35; column 10, lines 40-57; column 12, lines 52-53 and column 13, line 59 to column 14, line 4).

However, Butler et al fail to teach that the surface modification layer comprises at least a first moiety having the structure -Si-R^1 and a second moiety having the structure Si-L-R^2 and wherein R^1 is a chemically inert moiety selected from the group consisting of C_3 to C_{30} alkyl and benzyl optionally substituted with 1 to 5 halogen atoms, L is a linking group, R^2 is a hydrophilic moiety.

Lefkowitz et al reference discloses the step of derivatizing a glass substrate with two compositions, n-decyltrichlorosilane (NTS) and undecenyltrichlorosilane (UTS) to produce two silanes, -Si-R^1, and -Si-(L)n-R^2 wherein n is 1 wherein R^1 is chemically inert, and wherein R^1 is an alkyl group in the range of 2 to 24 carbon atoms, and may be benzyl, either unsubstituted or substituted with 1 to 5 halogen atoms, wherein L is a linker, and wherein R^2 comprises a functional group selected

from hydroxyl groups, carboxyl groups, amino group and thiol groups, preferably hydroxyl groups (column 2, lines 56-67; column 3, lines 10-23; column 6, lines 42 to column 7, line 58; column 9, lines 45-51 and figure 1), wherein R^1 moieties reduce surface energy and R^2 moieties comprise functional groups enabling attachment of molecular moiety of interest (column 3, lines 34-38). Lefkowitz et al. disclose that second silane (i.e. R^2) enables binding with intact oligomers (see abstract) which include polypeptides (column 4, line 64). Also, note that inert group R^1 and hydrophilic group R^2 of Lefkowitz et al are the same as the R^1 and R^2 of present application (for example, see specification, page 14, lines 22-34 and page 16, lines 8-10, wherein R^2 may be hydroxyl, carboxyl, amino, amide, preferably hydroxyl group) which are expected to interact non-covalently with biomolecules (e.g. proteins) in a similar manner i.e. non-covalent interaction of proteins is inherently present with this derivatized substrate as claimed in present application.

Lefkowitz et al also disclose that this derivatized substrate surface (non patterned) is particularly useful to fabricate an array for its reduce surface energy that constrain droplets of liquid and for its less processing and cost-effective considerations as compared to other patterned substrate (i.e. separated hydrophilic and hydrophobic zones or spots) surface that require considerable processing and are costly to prepare (column 1, line 60 to column 2, line 22).

Therefore, given the above fact that derivatized substrate with silane having inert and hydrophilic group is know in the art for fabrication of an array and are useful for its reduce surface energy to constrain applied droplets and for its ease of processing

and cost, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method and apparatus of Butler et al with the step of derivatizing a glass substrate with two compositions, n-decyltrichlorosilane (NTS) and decenyltrichlorosilane (UTS) to produce two silanes, -Si-R^1 and -Si-(L)n-R^2 wherein n is 1, wherein R^1 is chemically inert, and wherein R^1 is an alkyl group in the range of 2 to 24 carbon atoms, and may be benzyl, either unsubstituted or substituted with 1 to 5 halogen atoms, wherein.L is a linker, and wherein R^2 comprises hydophilic group, as taught by Lefkowitz et al, in order produce cost-effective substrate surface for arrays that requires substantially less processing time and have reduce surface energy to constrain droplets of liquid applied to a substrate surface, with a reasonable expectation of success. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of derivatizing a glass substrate with two compositions, n-decyltrichlorosilane (NTS) and decenyltrichlorosilane (UTS) to produce two silanes, -Si-R^1 and -Si-(L)n-R^2 as taught by Lefkowitz et al, in the method and apparatus of Butler et al, since Butler et al teach that the support substrate can be glass (see column 9, lines 26-27), and the silanes of Lefkowitz et al are also derived on glass substrates.

With regards to claims 8-9, Butler et al teach between 10-500,000 sites (at least 250 solutions). See column 6, line 8.

With regards to claims 16-17, Lefkowitz et al teach that the second silane, UTS, is 2.5 wt.% (i.e. about 0.5% to about 30% of the modificatiop layer). See column 9, lines 45-50.

With regards to claims 18-19 Lefkowitz et al teach that R^2 may be a functional group such as hydroxyl,

carboxyl, thiol and amino. See column 6, lines 42-46 and column 7, lines 49-50.

5. Claims 2-6 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butler et al (US 6,589,726 B1) in view of Lefkowitz et al (US 6,258,454 B1) as applied to claim 1 above, and further in view of Haab et al (Genome Biology, 2001).

Butler et al and Lefkowitz et al references have been disclosed above, but fail to teach the step of further drying the substrate after depositing the solutions.

Haab et al reference teaches the step of drying glass microscope slides for 1 hour at 80°C in a vacuum oven, in order to produce antibody/antigen immobilized slides. See page 12, left column, 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Butler et al and Lefkowitz et al with the step of drying glass microscope slides for 1 hour at 80°C in a vacuum oven, as taught by Haab et al, in order to produce antibody/antigen immobilized slides. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of drying slides immobilized with antibodies or antigen, as taught by Haab et al, in the method of Butler et al and Lefkowitz et al, since Butler

et al and Lefkowitz et al teach proteins immobilized on glass slides, and the antibody of Haab et al is one type of protein that is also immobilized on glass slides.

With regards to claims 3-6 and 13, Haab et al teach a blocking solution of 3% non-fat milk/PBS/0.02% sodium azide. See page 12 right column, 1st paragraph. In addition, with respect to claim 4, since blocking solution is placed on the entire slide, the hydrophobic sites (i.e. intervening areas) are subjected to non-covalent binding.

6. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Butler et al (US 6,589,726 B1) in view of Lefkowitz et al (US 6,258,454 B1) as applied to claim 11 above, and further in view of Silzel et al (Clinical Chemistry, 1998).

Butler et al and Lefkowitz et al references have been disclosed above, but fail to teach that each discrete site is in the range from 30 to 150 micrometers in diameter.

Silzel et al reference teaches jet-printed spots of antibody reagent having diameters of 100 um, in order to reduce the size of binding assays for reduced costs, faster chemistry, and equivalent or improved sensitivity. See page 2036, left column, last paragraph.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Butler et al and Lefkowitz et al with jet-printed spots of antibody reagent having diameters of 100 um, as taught by Silzel et al, in order to reduce the size of binding assays for reduced costs, faster chemistry, and equivalent or improved sensitivity. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including spots of

antibody reagent having diameters of 100um, as taught by Silzel et al, in the apparatus of Butler et al and Lefkowitz et al, since Lefkowitz et al teach molecule deposition by jet-printing techniques, and the antibody of Silzel et al is one type of molecule that can be deposited by jet-printing techniques.

Response to Argument

7. Applicant's arguments filed 9/26/05 have been fully considered, but they are not persuasive to overcome the rejections under 35 USC 103.

Applicants argued that Butler et al do not teach or suggest "at least two solutions, each solution comprising a probe protein", which is not convincing as Butler et al disclose depositing biological entities on hydrophilic sites of the substrate (column 8, lines 9-10) and the biological entities may be protein (column 14, lines 4-5 wherein, in protein-protein interaction, and probes attached to substrate are protein probes) and "at least two solution comprising a probe protein" are inherently present in array fabrication method (drop-on-demand) wherein, protein probes are deposited onto discrete sites. With regards to non-covalent interaction, both Butler and Lefkowitz disclose hydrophilic groups (e.g. amino, hydroxyl, carboxyl, thiol and amido) for binding to biomolecules and these hydrophilic groups are the same as the hydrophilic groups of present application and thus are expected to interact with proteins non-covalently as claimed in present application.

Applicant's arguments that Butler et al's array are patterned with hydrophilic and hydrophobic sites are accurate; however, for features of surface modification layer

comprising "at least a first moiety ---- and a second moiety ---- wherein R1 is a chemically inert moiety ----- R2 is a hydrophobic moity", Lefkowitz et al as secondary references have been relied upon.

Applicants must realize that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fines, 837 F.2d 1071, 5USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case Lefkowitz et al also disclose that this derivatized substrate surface (non patterned) is particularly useful to fabricate an array for its reduce surface energy that constrain droplets of liquid and for its less processing and cost-effective considerations as compared to other patterned substrate (i.e. separated hydrophilic and hydrophobic zones or spots) surface that require considerable processing and are costly to prepare (column 1, line 60 to column 2, line 22). With this motivating disclosure, one of ordinary skill in the art would obviously be motivated to modify the substrate surface of Butler et al with the derivatized support as taught by Lefkowitz et al, in order produce cost-effective substrate surface for arrays that requires substantially less processing time and have reduce surface energy to constrain droplets of liquid applied to a substrate surface, with a reasonable expectation of success.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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